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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,400	03/30/2001	Yehuda Shoenfeld	01/21885	1174

30623 7590 03/25/2009

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
03/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/806,400	SHOENFELD ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/6/09 and 1/22/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 1/6/09 and 1/22/09 has been entered.

2. Claim 28 is under consideration.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 28 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed method of treating atherosclerosis using oxidized LDL. The specification does not disclose how to use the claimed method in vivo in humans to treat disease. Applicant has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the treatment of disease in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence as to how the instant invention could be used for treating atherosclerosis using oxidized LDL.

Judge Lourie stated in Enzo Biochem Inc. v. Calgene Inc. CAFC 52 USPQ2d 1129 that:

The statutory basis for the enablement requirement is found in Section 112, Para. 1, which provides in relevant part that:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. . . .

35 U.S.C. Section 112, Para. 1 (1994). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " Genentech, Inc. v. Novo Nordisk, A/S , 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright , 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see Hybritech, Inc. v. Monoclonal Antibodies, Inc. , 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), which in this case is October 20, 1983 for both the '931 and '149 patents. 8 We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., Wands , 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In In re Wands , we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See Amgen, Inc. v.

Chugai Pharm. Co., Ltd. , 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Regarding Wands factors (4) and (8), the claims encompass treatment of atherosclerosis in vivo in humans. Regarding Wands factors (5) and (7), there is a high degree of unpredictability in the art. For example, Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Similarly, the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Thus, it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. Regarding Wands factor (3), while the specification provides an example in a mouse model, there were copious amounts of mouse research that suggested that oral tolerance could be used to treat MS or rheumatoid arthritis, yet said diseases were not successfully treated in humans using oral tolerance. Regarding Wands factor (2), there is no disclosure in the specification as to what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism.
Based on the aforementioned undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification.

Regarding applicants comments and the Dorats declarations, Spack teaches that attempts to treat MS via inducing oral tolerance to myelin protein have been unsuccessful (see abstract). Similarly, the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Thus, it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. Furthermore, applicants ***own publication*** (George et al., 2004) states (*5 years after the filing date of the instant application*) that: “The application of oral tolerance as a therapeutic strategy has proven successful in various immune and non-immune mediated *experimental models*, *yet efficacy in human disease is still pending*.”. **It is noted that animal model**

used in said publication is essentially the same model as disclosed in the specification.

Thus, the Inventors comments in George et al. indicate that it is recognized in the art that it is unpredictable whether human disease can be treated via inducing oral tolerance to a disease antigen. George et al. would therefore also indicate that the model used in their publication was not necessarily predicative of efficacy in humans.

While the claim does not recite a specific mechanism of action, the disclosure in the specification indicates that the claimed method works via oral tolerance. Furthermore, the model used in the specification is essentially the same as disclosed in George et al. wherein George et al. address their treatment as a form of oral tolerance.

Regarding applicants comments about animal models, there were a plethora of animal models used to treat MS and RA like diseases, yet Spack teaches that attempts to treat MS in humans via inducing oral tolerance to myelin protein have been unsuccessful (see abstract) and the art recognizes that attempts to treat rheumatoid arthritis via inducing oral tolerance to collagen have been unsuccessful (see McKown et al.). Regarding Wands factor (3), while the specification provides an example in a mouse model, there were copious amounts of mouse research that suggested that oral tolerance could be used to treat MS or rheumatoid arthritis, yet said diseases were not successfully treated in humans using oral tolerance. Regarding Wands factor (2), there is no disclosure in the specification as to what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism. Regarding applicants comments, page 19 of the specification refers to doses given to mice in a prophetic experiment for which no results were provided. Thus, it is unclear as to whether a particular dosage actually had any effect. The specification, page 18 refers to a single dosage given to mice. There is no disclosure in the specification as to dosages to be used in humans or what doses would be used to induce the functional parameters recited in the claim which are related to properties of the oral tolerance induction mechanism. Yesair et al. teach a composition for oral administration containing LPC (see column 5, last paragraph and Examples). LPC is also a derivative of ox ldl (see specification, page 5, first complete paragraph). LPC is a modified LDL. The specification discloses that LPC has the

properties of ox ldl. The specification, page 11, fourth paragraph *discloses that LPC can be used in the previously claimed method*. Yet the Harats declaration (12/18/03) discloses that LPC and other forms of modified LDL cannot be used in the claimed method (see sections 7-9). In addition, the specification discloses that: *"Lysophosphatidylcholine (LPC) is expressed in human atherosclerotic plaques. It is an active biological substance that can induce the first steps of atherogenesis. Indeed it is even more potent than Ox LDL."(*see page 5, penultimate paragraph).

Thus, even though LPC is involved in the pathogenesis of atherogenesis, oral tolerance to LPC cannot be used to treat atherosclerosis. Regarding the Harats declaration (12/18/03) and the LDLR mice model, Wouters et al. discloses that the LDLR mouse displays cholesterol metabolic pathways not found in humans (see page 474, second column, second paragraph)) and as a consequence "This route can serve as a backup mechanism for lipoprotein clearance in ldlr mice, yielding unforeseen side effects "(page 474, second column, first paragraph).

Regarding the various cited publications, while said publications may use the animal model under consideration, none of said publications disclose that the "likelihood of new molecules to work as anti-atherosclerosis drugs in humans is high". Furthermore, none of said publications address said model in the context of oral tolerance and the failure of animal models of oral tolerance to predict efficacy in humans. In addition, none of said publications disclose an *untested* drug that was later found to have efficacy in humans.

5. No claim is allowed.

6. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
Primary Examiner, Art Unit 1644